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Food and Drug Administration
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MERCK
Research Laboratories

RE: [Docket No. 98D-1266]
Draft Guidance on Placing the FDA Therapeutic Equivalence Code on Prescription Drug Labels and Labeling

Merck & Co., Inc, is a leading worldwide, human health product company. Merck's corporate strategy -- to discover new medicines through breakthrough research -- encourages us to spend more than $2 Billion, annually, on worldwide Research and Development (R & D). Through a combination of the best science and state-of-the-art medicine, Merck's R & D pipeline has produced many of the important pharmaceutical products on the market, today.

Research, by its nature, is a multidisciplinary and highly risk-intensive business. It depends upon many variables, including: prolific source materials, first class talent, adequate funding, efficient and effective quality processes and procedures, and a predictable regulatory environment.

Merck's research scientists ensure that our Research process continues to identify medically important product candidates from thousands of chemical and molecular entities screened, each year. Only one in ten of these research product candidates is selected to enter the Development testing programs. The medicines, which Merck ultimately presents to worldwide health authorities for marketing approval, are those that have met the highest technical standards available and those that are able to withstand the most critical regulatory review.

Merck supports regulatory oversight of product development that is based on sound scientific principles and good medical judgment. Regulators must be reasonable, unbiased and efficient when they review the quality, effectiveness and safety of our products. It is in both of our interests to see that important therapeutic advances reach patients without unnecessary or unusual delays.

In the course of bringing our product candidates through developmental testing, clinical trials, and market research, Merck regularly identifies issues and/or problems affected by this proposal. Indeed, we are committed to bringing safe products to market, which includes using the most informative and concise labels and labeling available. For these reasons, we are very interested and well qualified to comment on this FDA guidance that would allow a generic drug manufacturer to place the therapeutic rating provided in the *Approved Prescription Drug Products with Therapeutic Equivalence Evaluations List* (herein after referred to as the *Orange Book*) on product container labels, and/or drug product labeling.

98D-1266

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General Comments on Proposed Rule

While we commend the FDA for trying to provide information to assist the health professional in determining whether a specific drug product is therapeutically equivalent to another pharmaceutically equivalent drug product, Merck has serious concerns about this policy as written.

We have several specific comments on the guidance, as outlined below:

Guidance Comment; Sections III, IV and VI:

In this guidance, the Agency suggests the use of voluntary system in accordance with the *Orange Book* to label generic prescription products with an equivalence code. The proposed code is a two-letter system that will be added to the container and/or carton label for each generic product. This code is designed to designate whether a particular generic drug is "therapeutically equivalent to other pharmaceutically equivalent products (first letter) and to provide additional information on the basis of FDA's evaluations (second letter)." The primary container and/or carton label would be revised to include the two-letter designation and provide the trademark information for the innovator product. For example, the generic version of ALDORIL® would be labeled as follows:

Methyldopa and Hydrochlorothiazide Tablets, USP
250 – 15 mg

AB to ALDORIL®

ALDORIL is a registered trademark of Merck & Co., Inc.

Merck Comment:

Merck is concerned that no definition of the two-letter code on the labeling will be provided. Thus, addition of this text to the label without definition would still require that the healthcare professional refer to the Orange Book for clarification of equivalence, so the advantage of adding this code to the labeling would be extremely limited.

Guidance Comment; Section V.:

"With the repeal of section 301 (1) in the Modernization Act, the Agency believes that any legal arguments that therapeutic equivalence ratings should not be used in the labeling are moot."

Merck Comments:

Inclusion of the therapeutic equivalence code on the labels and labeling for prescription drugs could be misleading as it could imply therapeutic equivalence for the generic versus the innovator product. In addition, the code could also imply that the generic version of the innovator product is actually manufactured or endorsed by the innovator company. As a result of these implications, inappropriate substitutions could result (eg. a patient could receive the generic product when the innovator product should have been dispensed) which may lead to patient safety issues upon the product substitution. These issues regarding perceived endorsement and therapeutic equivalent could also place the innovator company at increased liability.

Guidance Comment; Section V.:
"Although nothing would prohibit the placing of the therapeutic equivalence rating in the package insert labeling, we believe that the most appropriate placement is on the immediate container and carton labeling where it is easy to see. This information may assist the health professional in determining whether a specific drug product is therapeutically equivalent to another pharmaceutically equivalent drug product."

MRL Comments:
Merck is concerned that the changes to the label that include this type of additional information may be a source of product confusion to the consumer receiving product dispensed in the original container (Unit-of-Use Containers) as the consumer would not be aware of its intent.

In addition, the FDA recently issued guidelines addressing readability of product labels. They mandated replacement of the statement "Caution Federal law prohibits dispensing without prescription" with "Rx only." This initiative was undertaken to provide more available space on primary container labels to decrease product confusion. Initially it was requested that this be completed industry-wide within 180 days. To now request the addition of a minimum of two additional lines of text on the primary container label is counter to the intent of the previous mandate. Merck believes that Agency recommended these changes to the label for valid reasons and thus believes that the Agency should review this earlier decision prior to taking any further action with regards to this guidance document.

Furthermore, with regard to several generic products, there may be more than one trademark for the innovator product, eg. lisinopril. The label for generic lisinopril would have to include trademark information for Merck & Co., Inc. for PRINIVIL® as well as trademark information for Zeneca Pharmaceuticals for ZESTRIL®. Inclusion of this amount of text again brings up the issue of the available space on primary container label.

Guidance Comment; Section V. (footnote):
Certain trademark law has established that "[a] manufacturer does not commit unfair competition merely because it refers to another's product by name in order to win...." "....*G.D. Searle & Co. v. Hudson Pharmaceutical Corp., 715*.....[wherein the court stated that the defendant could continue to use the brand name METAMUCIL® on its generic product provided the trademark appeared in the same type size as the other words on the label, the trademark registration symbol "®" was used with the METAMUCIL® trademark and a disclaimer was added stating that there is no association between the generic product and METAMUCIL®]....."

Merck Comments:
It is important to note that the Lanham Act prohibits use of a registered mark in interstate commerce without the permission of the registrant if such use is likely to cause confusion, mistake, or to deceive as to the source or origin of the goods in question. 15 U.S.C. § 1114(1). The Lanham Act unfair competition section carries the same standard. 15 U.S.C. § 1125(a)(1). Thus, Merck is troubled that the Guidance proposes the use of a mark in interstate commerce without the permission of the *registrant.* The critical element is whether there is likelihood of confusion, mistake or deception. Likelihood of confusion arises when an appreciable number of ordinarily prudent

purchasers are likely to be confused, mistaken, or deceived as to the source or origin of the product. The following are several reasons why Merck believes that the likelihood of confusion will arise.

The FDA position appears to be that a mere acknowledgment of the ownership of a trademark is a disclaimer, and with a disclaimer there is no likelihood of confusion. We do not believe this is accurate. Disclaimers in themselves are not dispositive with respect to eliminating consumer confusion. In some cases the courts have accepted that under certain circumstances a disclaimer can avoid the problem of infringement, but to be effective the disclaimers must clearly state the true facts and use of the mark must not be an attempt to "trade off" on the goodwill of the mark. There are circumstances when a disclaimer will not be sufficient to avoid confusion, mistake, or deception as to the source or origin of the product.

Merck also believes the mere reference to ownership of a mark is not a disclaimer and does not significantly reduce the likelihood of confusion otherwise caused by the use of another's mark. Even in the G.D. Searle & Co. v. Hudson Pharmaceutical Corp case, that involved over-the-counter products, the Court of Appeals approved the statement by the court below to make it clear to REGACILIUM® purchasers not only that METAMUCIL® is a Searle product, but also that REGACILIUM® is not. The text approved was "METAMUCIL® is made by G. D, Searle & Co. Searle does not make or license REGACILIUM®." The proposed Guidance does not require any such statement. The potential confusion, as to whose product this is, would not be clarified by the FDA suggested statement of who owns the trademark.

It must be recognized that for a prescription drug product, confusion can take place at the pharmacist level and also at the patient level. The appearance of another party's trademark on the product packaging and labeling will likely confuse both the pharmacist and the patient. Use of the code letters with the trademark will not be clearly understood and will likely lead to misunderstanding that this is the branded product by both the pharmacist and patient. Clearly, patients receiving a unit-of-use package with "AB to CHICOSE" will have no idea what "AB" means and will easily understand this to be the "CHICOSE" brand product.

It should also be noted that many generic products do not use a product trademark. In such case, the only product trademark appearing on the packaging and labeling will be that of another company. This is very likely to cause confusion and mistake. Certainly, a pharmacist only seeing the brand "CHICOSE" on the packaging could be mislead into putting "CHICOSE" on the label he prepares for the patient container and the patient will understand this to be the "CHICOSE" product.

As discussed earlier, the draft Guidance appears not to require that if there are multiple manufacturers with different trademarks for the product, that all marks must be referenced. Merck is concerned that if only some trademarks are referenced, but not all, will this be understood that the products for the omitted marks do not meet the standard for "AB to"? We believe such omission can be a source of confusion leading to incorrect judgments.

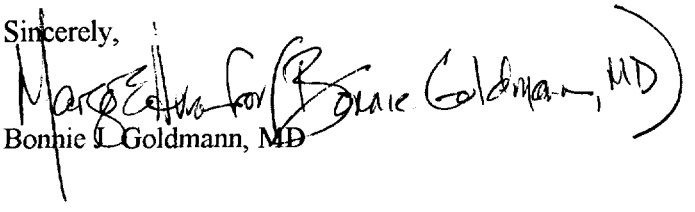
For the reasons stated above, we believe use of another's trademark as proposed in the draft Guidance will likely cause confusion, mistakes, and deceive as to the source or origin of the product and will constitute trademark infringement. There is no health or safety needs requiring this use of

another's trademark. And most importantly, the generic product is accurately identified by use of the official USAN for the product that *also* appears on the branded product.

Summary –
Forthrightly, Merck is having difficulty understanding the problem that this guidance is attempting to correct since the information on therapeutic equivalence is readily available in print and on the FDA web page. Moreover, the use of the equivalence code may lead to inappropriate substitution, which could result in increase risk to the patient. Given these concerns and the current availability of this information to Healthcare professionals, we respectively disagree that this proposed guidance has added value to the health and safety of the public and propose that the Agency re-evaluate alternatives to educate the Healthcare professional regarding therapeutic equivalence.

We welcome the opportunity to comment on this draft guidance and, if appropriate, to meet with you to discuss these issues.

Sincerely,



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